DETAILED ACTION

Response to Arguments

1. Applicant's arguments filed on February 19, 2008 have been fully considered but they are not persuasive. The applicant's argument stating that Duveneck fails to disclose a excitation source containing chemical/biological excitation medium which flow through the inlet opening was not found persuasive (see applicant's argument on page 45). The examiner respectfully disagrees with the applicant because as stated in the previous office action dated 11/01/2007 page 4, the Duveneck reference discloses an excitation source (origin or a place where something begins) containing chemical/ biological excitation medium(liquid containing luminpohore or luminescence substance(chemical) to be detected, the liquid containing the luminescence substance is coming from a source into the device via the inlet (see previous office action page 4) and also the applicant does admit on page 51 that Duveneck col. 21, lines 10 -14 discloses a sample which is supplied via the inlet contains luminescent substance. Furthermore the applicant's argument that the Schurmann-Mader reference does not qualify as prior art under 102(a)/103 obviousness rejection because the applicant has foreign priority dates of March 27, 2002 and July 26, 2002 was not found persuasive because Schumann-Mader qualifies as 102(a) prior art since it has a publication date before the effective US filing date (3/5/2003) of the applicant's invention. The applicant's argument that Siegen is not prior art because it and the applicant's current invention were commonly owned by Micronas Intermettal GmbH at the time of the invention was not found persuasive since the above argument applies only to a 102(e)/103 art rejection and the Sieben

reference is available under 102(b). Additionally the applicant's argument that the amendment to the claims overcomes the prior art rejection was not found persuasive, see the rejection below.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 2, and 4-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duveneck (US 6,469,785) in view of Rokugawa (US 4,621,059).

Regarding claim 1,Duveneck disclose a device for detecting a luminescence event in, at, or in the immediate vicinity of a cell, a cell cluster, or a tissue, said device comprising: having

(a) a carrier element (76) with a surface (7) prepared for direct or indirect coupling of cells,

(b) a detector (detection unit 4 in the form of a photodiode) for receiving a luminescence signal indicative of the luminescent event, where the detector is integrated into the carrier element below surface,

(c) a cover (2) covering surface covering the prepared surface to form a cavity(68), the cover having an inlet opening(64) and an outlet opening(66), and

(d) an excitation source containing chemical/biological excitation medium (liquid containing luminpohore or luminescence substance to be detected) which flows through the inlet opening (64).(see Duveneck fig 1 and 8, col. 5 lines 13- 27, 53-58 line65 - col. 6 line 14, col. 6 lines 48 - lines 67; col. 7 lines 5 -12, col. 8 lines 26 - 38, col. 17 lines 59 - 67, col. 19 lines 25 -59, col. 21 lines 10 - 14, lines 42 - 56 and col. 22 lines 15-20). However, Duveneck fails to disclose an excitation source connected to the inlet opening of the device. Rokugawa (US 4,621,059) discloses a device for detecting luminescence

where in an excitation source (12) containing biological/chemical excitation medium and connected to the inlet opening (see Rokugawa fig 1 col. 2 lines 17 - 28, col. 3 lines 21 - col. 4 line 68). It would have been obvious to one having ordinary skill in the art at the time of the invention to have the excitation source be connected to the inlet opening of the device of Duveneck as taught by Rokugawa since it was known in the art at the time to do so and furthermore, since it has been held that forming in one piece an article which has formerly been formed in two pieces and put together involves only routine skill in the art.

Additionally, the phrase " accepting a biological or chemical excitation medium that includes a luminophore, where the excitation medium influences the metabolism of the cell during excitation thereof...the luminescence signal " is intend use of the excitation source and phrase does not further limit the claim and the device as claimed is capable of the applicants intended use.

Regarding claim 2, the combined reference as applied to claim 1 above discloses the device according to claim 1 in which a optical filter (636) is located between prepared surface (609) and the optical detector (604) (see Duveneck col. 16 lines 46 - 62).

Regarding claim 4, the combined reference as applied to claim 1 discloses the device of claim 1, in which multiple detectors are integrated into carrier element below the surface prepared for coupling the cells (see Duveneck fig. 1(detection unit could be an array of detector) fig 5, col. 5 lines 53 - 56; col. 6 lines 48 - 49; col. 13 lines 21 - 31)

Regarding claim 5, the combined reference as applied to claim 4, disclose the device according to claim 4, in which detector comprises a photodiode (see Duveneck col. 6 lines 48 - 49).

Regarding claim 6, the combined reference as applied to claim 1 discloses device according to claim 1, comprising an evaluation circuit (circuits for driving the photoelectric detectors (detector which detects light / luminescence intensity and converts it into corresponding electrical signals and a measurement of the activity on the sensing surface is obtained or evaluated) connected to at least one detector (see Duveneck col. 3 lines 42 - 44 and lines 50 -52).

Regarding claim 7, the combined reference as applied to claim 6 above discloses the device of claim 6, in which the evaluation circuit is integrated into the carrier element (the circuit for driving the detector are produces on the same substrate (carrier); see Duveneck col. 3 lines 42 - 44 and lines 50 -52).

Regarding claim 8, the combined reference as applied to claim 6 above discloses the device of claim 6. The combined reference fails to disclose the device of claim 6 in which the excitation source controlled by the evaluation circuit tends the chemical or biological substance to the inlet opening (8). Rokugawa (US 4,621,059) further discloses a biosensor having a source (12) controlled by a circuit (control valve (8)) to

send substance from the source (12) to an inlet opening (see Rokugawa fig., col. 3 lines 20 -23). It would have been obvious to one having ordinary skill in the art at the time of the invention to have the excitation source be controlled by the circuit of the combined reference as taught by Rokugawa in order to make dispensing of substance from the source automated and further more since, it was well known in the art at the time to have a source be controlled by a circuit.

Regarding claim 9, the combined reference as applied to claim 8 discloses the device according to claim 8. The combined reference fails to disclose the device of claim 8, in which a valve is disposed in an inlet line between the excitation source and inlet opening to control the supply of medium. Rokugawa (US 4,621,059) further discloses a biosensor having a source (12), a control valve (8) disposed between the source (12) and the inlet (see Rokugawa fig., col. 3 lines 20 -23). It would have been obvious to one having ordinary skill in the art at the time of the invention to have a valve disposed between the inlet and the source of the combined reference as taught by Rokugawa, since, Rokugawa states on lines 22 -23 that such a modification would aid in the regulation of the quantity of the substance from the source that is added/dispensed to the inlet.

Regarding claim 10, the combined reference as applied to claim 1 above discloses the device according to claim 1,wherein an adhesion matrix (adhesion promoting layer is

applied to a waveguide surface) and/or a growth substrate for cells is applied to the surface (see Duveneck col. 18 lines 50 - 52).

6. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Duveneck (US 6,469,785) in view of Rokugawa (US 4,621,059) as applied to claim 1 above, and further in view of Sieben et al (US 6,104,495).

Regarding claim 3, the combined reference as applied to claim 1 above discloses the device of claim 1. However, the combined reference fails to disclose the device of claim 1 in which the carrier element is a semiconductor body. Sieben et al (US 6,104,495) discloses a device for detecting signals related to chemical or physiological condition in cells immobilized on a sensing surface attached to semiconductor body (semiconductor material) carrier (see Sieben abs, col. 1 line 53 - col. 2 line 7; col. 3 lines 8 - 24). It would have been obvious to one having ordinary skill in the art at the time of the invention to use a semiconductor body as the carrier element in the device of the combined reference as taught by Sieben, since, Sieben states at col. 3 lines 11-13 that such a modification would allow for the use of conventional fabrication processes for integrated circuit on the carrier.

7. Claims12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duveneck (US 6,469,785) in view of Rokugawa (US 4,621,059) as applied to claim 1, and further in view of Schurmann-Mader et al (WO 2001/043875) .

Regarding claim 12, the combined references disclose the device according to claim 1 in which an immobilizing medium (8) is applied to the surface (7). However, the combined references fail to specifically teach that a cell-immobilizing medium is applied to surface. Schurmann-Mader (see US 2002/0182631 for English language equivalent) discloses that it is known in the art to apply cell-immobilizing medium to a sensing surface (a layer is deposited on the surface (base plate) for the immobilization of biological recognition elements such a whole cells or fragments of cells) (see the US equivalent case (US 2002/0182631) of Schurmann-Mader paragraph [0052] and [0054]). It would have been obvious to having ordinary skill in the art at the to have an immobilizing medium be a cell immobilizing medium as taught by Schurmann-Mader since it was known in the art at the time to use such immobilizing medium on a sensing surface.

Regarding claim 14, the combined references as applied to claim 1 above, disclose the device according to claim 1 wherein chemical or biochemical recognition element are immobilized on the sensing surface. However, the combined references fail to disclose the device of claim 1 wherein at least one cell (6) is immobilized at the surface. Schurmann-Mader discloses that it is known in the art to immobilize biological or biochemical recognition elements such as whole cells on sensing surfaces (see US equivalent case (US 2002/0182631) of Schurmann-Mader paragraph [0054]). It would have been obvious to one having ordinary skill in the art at the time of the invention to

immobilize at least one cell on the surface of the combined references as taught by Schurmann-Mader since it was well known in the art at the time of the invention to do so.

8. Claims 11 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duveneck (US 6,469,785) in view of Rokugawa (US 4,621,059) as applied to claim 1 and 10 above, and further in view of Parce et al (5,278,048).

Regarding claim 11, the combined references as applied to claim 10 above, disclose the device according to claim 10. However, the combined references fail to disclose the device of claim 10 in which the growth substrate comprises gelatin. Parce (5,278,048) discloses a detecting/sensing device in which non-adherent cells may be grown on the surface of the sensor by mixing the cell with gelatin and then applying the mixture to the surface of the silicon sensor. It would have been obvious to one having ordinary skill in the art at the time of the invention to include a substrate such as gelatin in the device of the combined references as taught by Parce, since Parce states such substrates aid in adhesion of living cells to the sensing chamber and cells can be grown on such substrate (see col. 5 line s 60-co1.6 lines 11)

Regarding claim 15, the combined references as applied to claim 1 disclose the device according to claim 1. However, the combined reference fail to disclose the device of claim 1 in which a depression is created in the surface of the carrier device prepared for

receiving cells, by contrast with surface areas (101) not prepared for receiving cells, said depression being preferably at least 100 nm deep. Parce (5,278,048) discloses a detecting/sensing device in which a flow chamber has a surface with plurality of wells or depression. It would have been obvious to one having ordinary skill in the art at the time of the invention to create depressions on carrier surface of the combined references device as taught by Parce since Parce states at col. 2 lines 41-43 that such a modification would act to physically trap the living cell onto the surface by gravitational sedimentation. Further more, Parce discloses that the wells/depression should be of a sufficient width and depth to enable cells to remain in the chamber during ordinary flow rates (Parce col. 2 lines 44 - 46). It would have been obvious to one having ordinary skill in the art at the time of the invention to have the depressions be at least 100 nm deep, since it has been held that were the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art.

9. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Duveneck (US 6,469,785) in view of Rokugawa (US 4,621,059) and Schurmann-Mader et al (WO 2001/043875) as applied to claim 12 above, and further in view of Ikeda et al (US 5,582,697).

Regarding claim 13, the combined references as applied to claim 12 disclose the device according to claim 12. However, the combined references fail to disclose the device of

claim 12 in which the medium comprises negatively charged polystyrene. Ikeda (US 5,582,697) discloses that it is known in the art to use negatively charged polystyrene (polystyrene sulfonate) as an immobilization medium. It would have been obvious to one having ordinary skill in the art at the time of the invention to use negatively charge polystyrene as the immobilizing medium as taught by Ikeda since is known in the art for it hydrophilic properties.

10. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schurmann-Mader et al (WO 2001/043875) in view of Chappelle et al (US 4385113).

Regarding claim 16, Schurman-Mader discloses a method for detection of a luminescence event using a sensor, at, or in the immediate vicinity of a cell, a cell cluster, or a tissue, comprising: Immobilization of the cell at the surface prepared for receiving cells, introduction of a luminophore (luminescent dye or a luminescent nano-particle) in the vicinity of the cell, stimulation of the cell by a chemical or biological substance (the analyte), and detection of a luminescence signal (see the US equivalent case (US 2002/0182631) of Schurmann-Mader paragraphs [0011],[0017],[0023],[0028], [0054], [0106], [0122], [00127]). Schurmann- Mader fails to disclose the method of detecting a luminescence event wherein there is an induction of a luminophore, which reacts with a cell metabolic product in the cell or in the vicinity of the cell. However, Chappelle (US 4385113) discloses a method of detecting luminescence comprising inducing a luminophore (luciferase-luciferin mixture), which reacts with the cell or

bacteria metabolic product (ATP) resulting in a light/luminescence reaction related to the amount of ATP present (see Chappelle abs, col. 2 lines 41-47). It would have been obvious to one having ordinary skill in the art at the time of the invention to have the introduction of luminophore step include introducing a luminophore reacting with the cell metabolic product in the vicinity of the cell as taught by Chappelle in order to enable the sensor to measure the effect of cell affecting agent on the metabolic rate of the immobilized cell.

Regarding claim 17, the combined references as applied to claim 16 above disclose the method according to claim (15) 16, in which the luminescence signal is detected with temporal resolution (emission light from the measurement is measure time-resolved) (see the US equivalent case (US 2002/0182631) Schurmann-Mader paragraph [0019]).

10. Claims 18, 19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duveneck (US 6,469,785) in view of Sieben et al (US 6,104,495).

Regarding 18 and 22, Duveneck does discloses a device for detecting a cellular metabolic process associated with a cell by detecting a luminescence event in, at, or in the immediate vicinity of the cell, the device comprising: an immobilized surface or prepared surface, a detector for providing a luminescence signal indicative of the luminescent event, where the detector is integrated into the device below the cell; a cover that covers the prepared surface to form a cavity, the cover having an inlet and

an outlet; and an excitation source that provides to the cavity via the inlet a biological or chemical excitation medium that includes a luminophore.(see Duveneck fig 1 and 8, col. 5 lines 13- 27, 53-58 line65 - col. 6 line 14, col. 6 lines 48 - lines 67; col. 7 lines 5 -12, col. 8 lines 26 - 38, col. 17 lines 59 - 67, col. 19 lines 25 -59, col. 21 lines 10 - 14, lines 42 - 56 and col. 22 lines 15-20).

The Duveneck reference fails to disclose that the device comprises a semiconductive device with the surface prepared for coupling the cell thereto.

Sieben et al (US 6,104,495) discloses a device for detecting signals related to chemical or physiological condition in cells immobilized on a sensing surface attached to semiconductor body (semiconductor material) carrier (see Sieben abs, col. 1 line 53 - col. 2 line 7; col. 3 lines 8 - 24). It would have been obvious to one having ordinary skill in the art at the time of the invention to use a semiconductor body as the carrier element in the device of the Duveneck reference as taught by Sieben, since, Sieben states at col. 3 lines 11-13 that such a modification would allow for the use of conventional fabrication processes for integrated circuit on the carrier.

The above phrase "excitation medium influences the metabolism of the cell during excitation thereof by the medium, and where the luminophore reacts with a metabolic product of the cell during the excitation thereof to provide luminescence detected by the detector" is an intended use and does not further limit the claim.

Regarding claim 19, the combined references disclose the device of claim 18, further comprising an optical filter located between the prepared surface and the optical

detector, and where a plurality of optical detectors are integrated into the semiconductive substrate below the prepared surface (see Duveneck fig 1 and 8, col. 5 lines 13- 27, 53-58 line 65 - col. 6 line 14, col. 6 lines 48 - lines 67; col. 7 lines 5 -12, col. 8 lines 26 - 38, col. 17 lines 59 - 67, col. 19 lines 25 -59, col. 21 lines 10 - 14, lines 42 - 56 and col. 22 lines 15-20) .

11. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Duveneck (US 6,469,785) in view of Sieben et al (US 6,104,495) as applied to claim 18 above, and further in view of Rokugawa (US 4,621,059).

Regarding claim 20, the combined references of Duveneck and Sieben disclose the device of claim 18. The combined references fail to disclose the device of claim 18 in which the excitation source controlled by the evaluation circuit sends the chemical or biological substance to the inlet opening (8). Rokugawa (US 4,621,059) further discloses a biosensor having a source (12) controlled by a circuit (control valve (8)) to send substance from the source (12) to an inlet opening (see Rokugawa fig., col. 3 lines 20 -23). It would have been obvious to one having ordinary skill in the art at the time of the invention to have the excitation source be controlled by the circuit of the combined reference as taught by Rokugawa in order to make dispensing of substance from the source automated and further more since, it was well known in the art at the time to have a source be controlled by a circuit.

12. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Duveneck (US 6,469,785) in view of in view of Sieben et al (US 6,104,495) as applied to claim 18, and further in view of Schurmann-Mader et al (WO 2001/043875).

Regarding claim 21, the combined references of Duveneck and Sieben disclose the device according to claim 18 in which an immobilizing medium (8) is applied to the surface (7). However, the combined reference fails to specifically teach that a cell-immobilizing medium is applied to surface. Schurmann-Mader (WO 2001/043875) discloses that it is known in the art to apply cell-immobilizing medium to a sensing surface (a layer is deposited on the surface (base plate) for the immobilization of biological recognition elements such a whole cells or fragment of cells) (see the equivalent US Schurmann-Mader case (US 2002/0182631) paragraph [0052] and [0054] for English translation of WO). It would have been obvious to having ordinary skill in the art at the to have a immobilizing medium be a cell immobilizing medium as taught by Schurmann-Mader, since it was known in the art at the time to use such immobilizing medium on a sensing surface.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHANTA G. DOE whose telephone number is (571)270-3152. The examiner can normally be reached on Mon-Fri 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Walter Griffin can be reached on 571-272-1447. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GSD

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